

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
1 November 2001 (01.11.2001)

PCT

(10) International Publication Number  
**WO 01/80829 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K 9/00**
- (21) International Application Number: **PCT/US01/12805**
- (22) International Filing Date: **19 April 2001 (19.04.2001)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
**09/553,513** **20 April 2000 (20.04.2000)** **US**
- (71) Applicant: **BRISTOL-MYERS SQUIBB COMPANY**  
[US/US]; P.O. Box 4000, Route 206 and Provinceline  
Road, Princeton, NJ 08543-4000 (US).
- (72) Inventors: **CORBO, Michael**; 17 Litton Road, Flemington, NJ 08822 (US). **DESAI, Jatin**; 2009 Pheasant Hollow Drive, Plainsboro, NJ 08536 (US). **PATELL, Mahesh**; 4 Farrington Street, Edison, NJ 08820 (US). **WARRICK, Ronald**; 42 Route 523 South, Sergeantsville, NJ 08557 (US).
- (74) Agent: **KRIEGER, Stuart**; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— *without international search report and to be republished upon receipt of that report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



**WO 01/80829 A2**

(54) Title: **TASTE MASKING COATING COMPOSITION**

(57) Abstract: There is provided a coating composition that masks the undesirable taste of a pharmaceutically active ingredient, i.e. drug or medicine, that is consumed orally. The coating composition has polyvinyl acetate, and a dimethylaminoethyl methacrylate and neutral methacrylic acid ester. Optionally, an alkaline modifier may be included in the coating composition to enhance release of the active ingredient.

**TASTE MASKING COATING COMPOSITION****BACKGROUND OF THE INVENTION**5    **1. Field of the Invention**

The present invention relates to a coating applied to the outside of a pharmaceutically active ingredient. More particularly, the present invention relates to a coating that  
10 masks the taste of a pharmaceutically active ingredient.

**2. Description of the Prior Art**

In general, there are two types of tablet dosage forms that  
15 are available in the marketplace, one that can be swallowed as a whole entity and the other as a chewable tablet. If the tablet is swallowed whole, the unpleasant taste of the pharmaceutically active ingredient is greatly minimized or avoided altogether. However, tablets formulated in a chewable form are designed for  
20 young children and for people with difficulty swallowing. Hence, the undesirable taste of the chewable tablet is mainly due to the bad taste of the pharmaceutically active ingredient. This can ultimately create a feeling of reluctance to taking medicine.

The use of a coating as part of a medicament is known. The coating is typically applied for the ease of swallowing and provides a barrier, which prevents the undesirable taste of the drug ingredient from coming through, making the drug preparation more palatable. In addition, this type of coating can be designed to act as a time release mechanism to control the rate of release of the medicine in the body. This can be accomplished in various ways such as adjusting the thickness of the coating and selection of the coating polymers/components that are used in these types of specialized coating formulations.

Various types of coatings can be applied to the outside of tablets and drug powders to achieve a specific desired effect. Enteric coatings are designed to be soluble in the intestine, where the pH is 6.5 or higher, but insoluble in the stomach, where the pH is lower. On the other hand, reverse enteric coatings are designed to be partially soluble in the stomach, i.e. under acidic or lower pH conditions, thereby releasing the drug in the stomach. Coatings can also be used for masking purposes including taste masking of chewable products.

Several U.S. patents are directed to taste masking.  
However, none disclose the coating of the present invention.

U.S. Patent No. 4,851,226 issued on July 25, 1989 to Julian  
5 et al. It provides a chewable medicament tablet made from  
granules coated with a blend of cellulose acetate or cellulose  
acetate butyrate and polyvinyl pyrrolidone.

U.S. Patent No. 5,075,114, which issued on December 24,  
10 1991 to Roche, provides a taste masking and sustained release  
coating applied to a tablet. The coating blend is made with  
cellulose acetate and/or cellulose acetate butyrate and  
hydroxypropyl cellulose.

15 U.S. Patent No. 5,489,436 issued on February 6, 1996 to Hoy  
et al. This patent provides chewable tablets that have a  
coating consisting essentially of dimethylaminoethyl  
methacrylate and neutral methacrylic acid ester, and a polymer  
selected from the group consisting of cellulose acetate,  
20 cellulose triacetate, and mixtures thereof.

**SUMMARY OF THE INVENTION**

It is an object of the present invention to provide a coating or coating composition that coats a pharmaceutically  
5 active ingredient or particle and, thus, is part of a medicament.

It is another object of the present invention to provide such a coating that masks the undesirable taste, without  
10 delaying the availability, of the pharmaceutically active ingredients when consumed orally.

It is also an object of the present invention to provide such a coating that is substantially insoluble in water and in a  
15 neutral pH environment, e.g. the mouth.

It is still another object of the present invention to provide such a coating that rapidly breaks down in an acid  
environment, such as in the stomach, thereby releasing the drug.

20

It is yet another object of the present invention to provide such a coating that readily dissolves, yet the rate of dissolution can be modified based on the composition.

It is a further object of the present invention to provide a medicament comprising a pharmaceutical active agent and the coating.

5        It is a still further object of the present invention to provide such a medicament in a variety of forms.

It is a still yet a further object of the present invention to provide a pharmaceutical composition comprising one or more  
10    pharmaceutical active agents coated with the coating of the present invention, which has an alkaline component in the coat composition that enhances the performance of the coat.

To accomplish the foregoing objects and advantages, the  
15    present invention, in brief summary, is a coating composition that masks the taste of a drug ingredient or medicine taken orally. The composition has (a) polyvinyl acetate, and (b) a dimethylaminoethyl methacrylate and neutral methacrylic acid ester.

20

In another embodiment, the coating composition of the present invention not only masks the taste of the medicine, but readily dissolves at an enhanced rate in an acid environment. The coating composition of this embodiment has (a) polyvinyl

acetate, (b) a dimethylaminoethyl methacrylate and neutral methacrylic acid ester, and (c) an alkaline modifier.

#### DETAILED DESCRIPTION OF THE INVENTION

5

In the present application, a medicament is defined as a drug ingredient that is coated with a coating composition. Taste masking is defined as a perceived reduction of an undesirable taste that would otherwise be there.

10

The mouth is, for the most part, a neutral environment where the pH is about 7. One can mask the unpleasant taste of a drug by surrounding the drug ingredient, drug particle, or an agglomeration of drug particles with a coating composition that is insoluble in the mouth. The coating must be formulated to rapidly break down in the stomach to release the pharmaceutically active ingredient into the body. The present invention accomplishes this by providing a coating composition that effectively masks the unpleasant taste of a pharmaceutically active ingredient, i.e., drug or medicine, taken orally and immediately dissolves in an acidic pH environment, thereby releasing the pharmaceutically active ingredient in the stomach. Moreover, there is no noticeable after taste.

The coating composition of the present invention has a taste masking blend. The blend is (a) polyvinyl acetate, and (b) a dimethylaminoethyl methacrylate and neutral methacrylic acid ester. Additionally, the composition may include an alkaline modifier.

In a preferred embodiment, the present invention is a medicament having a drug ingredient, and a coating composition for masking the taste of the drug ingredient. The blend has (a) polyvinyl acetate and (b) a dimethylaminoethyl methacrylate and neutral methacrylic acid ester. Optionally, the coating composition of the medicament may have an alkaline modifier that enhances the release of the drug ingredient into one's body. That is, the inclusion of the alkaline modifier in the coating composition quickens the release of the drug ingredient in the stomach.

Polyvinyl acetate is the first component in the coating composition of the present invention. The polyvinyl acetate is insoluble in water. This property gives a composition containing polyvinyl acetate resistance to dissolution in the mouth. The polyvinyl acetate can be provided in its pure form or as a blend. BASF Corporation provides such a blend,



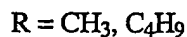
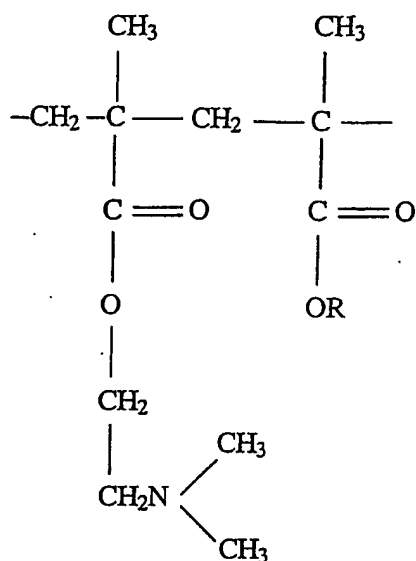
commercially available under the tradename KOLLIDON SR.

KOLLIDON SR is a blend that contains primarily polyvinyl acetate, polyvinylpyrrolidone, and minor amounts of sodium lauryl sulfate and colloidal silica.

5

The coating composition of the present invention includes about 3 percentage by weight or weight percent (wt.%) to about 97 wt.% of polyvinyl acetate of the total weight of the composition. Preferably, the polyvinyl acetate is included in an amount about 10 wt.% to about 70 wt.%, and more preferably, about 15 wt.% to about 50 wt.%. Above 50 wt.%, the polyvinyl acetate may be difficult to dissolve.

The dimethylaminoethyl methacrylate and neutral methacrylic acid ester is the second component in the present coating composition. This compound is available commercially from Rohm Pharma, and is sold under the tradename EUDRAGIT® E 100. EUDRAGIT® E 100 is supplied as colorless to yellow tinged granules with a characteristic amine-like odor. The structural formula is:



The dimethylaminoethyl methacrylate and neutral methacrylic acid ester is known to be soluble in acidic environments where the pH is up to about 5. At a pH greater than about 5, the ester is insoluble in water. Thus, the ester is relatively insoluble in the mouth where the pH is about 7.

The dimethylaminoethyl methacrylate and neutral methacrylic acid ester is in the present coating composition in an amount about 3 wt.% to about 97 wt.% of the total weight of the composition. Preferably, the dimethylaminoethyl methacrylate and neutral methacrylic acid ester is about 10 wt.% to about 40 wt.% of the total weight of the composition. The level of the

dimethylaminoethyl methacrylate and neutral methacrylic acid ester that is included in the coating composition is determined by considering the cost of the raw material and the desired dissolution rate. For example, below about 10 wt.%, the

5 dimethylaminoethyl methacrylate and neutral methacrylic acid ester does not dissolve as well as within the preferred range. Above 40 wt.%, the cost of this ingredient starts to become cost prohibitive.

10 The combination of the polyvinyl acetate and the dimethylaminoethyl methacrylate and neutral methacrylic acid ester has been found to mask the taste of the active ingredient.

In a preferred embodiment, an alkaline modifier may be

15 included in the coating composition of the present invention. The alkaline modifier serves several functions. It acts as a stabilizer, buffering the microenvironment of the coating to a neutral pH, which enhances the coating integrity over coatings that do not contain an alkaline modifier. This improves the

20 storage stability in a dry state or in a liquid suspension. The alkaline modifier, in a preferred embodiment, also functions as a plasticizer that reduces the brittleness of the coating. Moreover, it serves as a release modifier that increases the speed of dissolution of the coating in the acidic environment of

the stomach. This function allows a medicament coated with the present invention to deliver the drug ingredient to the system more rapidly than other systems. This provides another improvement over coatings that do not have an alkaline modifier.

5

The alkaline modifier enhances the controlled rate of release or break down or dissolving in the acid environment of one's stomach. Thus, a preferred coating composition that has (a) polyvinyl acetate, (b) dimethylaminoethyl methacrylate and  
10 neutral methacrylic acid ester, and (c) the alkaline modifier, has both taste masking and enhanced release properties that increases the speed of dissolution of the coating in the acidic environment of the stomach. Accordingly, the drug ingredient is delivered more rapidly than by a coat that does not have an  
15 alkaline modifier.

Suitable alkaline modifiers are, for example, triethanolamine (TEA), basic amino acids, talc, ammonium oleate, meglumine, trimethylamine, calcium silicate, aluminum magnesium  
20 silicate, food alkalizing agents that are commonly used in the food industry, or mixtures thereof. The basic amino acids can be, for example, L-arginine, L-histadine, prolamine, or mixtures thereof. Moreover, zein (corn protein) or aluminum magnesium

silicate may also be used in the present invention as an alkaline modifier.

An effective amount of the alkaline modifier may be added to the present coating composition. What is an effective amount varies according to the desired dissolution rate. The alkaline modifier is about 0.2 wt.% to about 20 wt.% of the coating composition. Preferably, the alkaline modifier is about 1 wt.% to about 15 wt.%, and more preferably, about 6 wt.% to about 12 wt.%.  
10 wt.%.

In one preferred embodiment, the alkaline modifier is about 2 wt.% to about 4 wt.% triethanolamine, and about 4 wt.% to about 8 wt.% other alkaline modifiers.

15 In another embodiment, the present coating composition may also have additives incorporated into the coating composition. Such additives are, for example, polyvinylpyrrolidone (PVP), 2-vinyl pyridine (V)/styrene (S) copolymer, cellulose acetate, and mixtures thereof. PVP is a polymer, which is soluble in water. In water, PVP will dissolve and break down, permitting the release of the medicine in the stomach. The 2-vinyl pyridine (V)/styrene (S) copolymer preferably has a polymer weight ratio of V to S of about 65/35 or 80/20.  
20

Ethyl cellulose may also be used as an additive in the coating composition. Preferably, the ethyl cellulose that is used, has a viscosity of about 5 to about 100 centipoise (cps) at 25°C, when made into a 2% solution. More preferably, the viscosity of the 2% solution of ethyl cellulose is about 30 to about 50 cps at 25°C. The ethyl cellulose is present in the coating composition in an amount about 10 wt.% to about 30 wt.%, preferably 20 wt.% to 30 wt.%.  
10

The coating composition may also have one or more optional ingredients. Such optional ingredients are diluents, fillers, bulking agents, pigments, opacifiers, other plasticizers including PVP, processing aids, or mixtures thereof.  
15

The present composition may also include typical processing aids. Such aids include, for example, sodium lauryl sulfate, colloidal silica, silicon dioxide, or mixtures thereof.

20 In a preferred embodiment, the coating composition of the present invention is about 28 wt.% polyvinyl acetate, about 28 wt.% dimethylaminoethyl methacrylate and neutral methacrylic acid ester, about 28 wt.% ethyl cellulose, about 5% talc, and about 3 wt.% to about 11 wt.% of other alkaline modifiers.

The ratio of the polymeric coating composition to pharmaceutical active ingredient is about 1:50 to 3:1.

Preferably, the ratio is about 1:10 to 2:1. Most preferably,  
5 the ratio is 1:10 to 1.5:1. The pharmaceutically active ingredient is present in an amount, which typically is about 0.1 mg to about 1000 mg per unit dose.

The coated medicament can be, for example, chewable  
10 tablets, powders for reconstituted suspensions, regular liquid form of prepared suspensions, fast dissolving quick melt tablets, lozenges, wafers, chewing gums, hard shell gelatin capsules with powder/granules/liquid fills, soft shell gelatin with liquid center or filled with powder or granules, regular  
15 compressed tablets with immediate or delayed release, candy and candy bar forms, aerosol creams and gels.

There are many pharmaceutically active ingredients that can be coated with the taste masking system and/or the taste masking  
20 and controlled release systems of the present invention. For example, the systems can be applied to analgesics such as acetaminophen, aspirin, ibuprofen, dexibuprofen lysinate, naproxen, ketoprofen; antibiotics such as lactams, quinolones, macrolides and salts thereof; gastrointestinal drugs such as

loperamide, famotidine, ranitidine, cimetidine and salts thereof; cardio vascular agents such as ibersartan, captopril, lisinopril and salts thereof; CNS drugs such as nefzodone, buspirone and salts thereof; antihistamines such as  
5 chlorpheniramine and astemizole; decongestants such as pseudoephedrine; cholesterol reducing agents such as statins; antivirals; anticancer; antiplatelet; vitamins; minerals; psyllium; or mixtures thereof.

10 A coated medicament may be prepared by using techniques and methods known in the art. For example, the coating composition of the present invention may be applied onto the drug active ingredient or medicine by using a fluidized bed coating operation.

15

To illustrate the present invention, the following examples are provided. However, it should be understood that the present invention is not limited to these examples.

20 In the examples, medicinal tablets were prepared as follows: (1) granules or crystals of a drug ingredient were coated with a coating composition in a fluid bed coater, (2) the coated granules or crystals were then combined with ingredients commonly used in making chewable/fast melting tablets and/or dry



suspensions such as sugars, sweeteners, and flavors, (3) the mixture was then compressed into tablet form to a hardness of about 10 Strong-Cobb units, using 11/16 inch round flat tooling. Each tablet had a weight of about 1550 mg.

5

Taste masking effectiveness is difficult to quantify. As set forth above, taste masking is understood to mean herein a perceived reduction of an undesirable taste that would otherwise be present. The examples demonstrate the taste masking benefits of the present invention, by measuring the percentage of a drug ingredient dissolved over a period of time under different pH conditions.

15

**EXAMPLE 1**

Coating (A) made of 27.78% KOLLIDONE SR, 27.78% Ethyl Cellulose, 28.0% Eudragit E® 100, 11.44% EASTMAN 9-45 (Acetylated Monoglyceride), and 5% Talc was applied to a drug ingredient, such as granules of acetaminophen (APAP) or caffeine powder. The coated drug ingredient was then compressed into tablet form, forming medicinal tablets that were then subjected to dissolution testing in solutions having a pH of 7 and a pH of 1.2.

Tables 1 and 2 show the percentage of a drug ingredient dissolved over a given period of time in an environment where the pH is about 7, i.e. conditions similar to the mouth, and in an environment where the pH is about 1.2, i.e. conditions similar to the stomach.

**TABLE 1****APAP with 30% Coating Add On of Coating A**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	4.9	4.9
6	22	45.6
11	32.4	61.9
16	42.1	71.5
21	51.2	77.8
26	59.8	81.6
31	67.3	85.3
36	73.8	87.8

10

**TABLE 2****Caffeine with 30% Coating Add On of Coating A**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	2.1	6.1
6	22.7	77.5
11	37.2	90.6
16	52.2	92.3
21	65.2	92.7
26	74.7	92.2
31	81.1	93.2
36	85.5	93.5

The results indicate that dissolution is hindered by coating (A), in an environment where the pH is about 7, and dissolution is quicker in an environment where the pH is about 1.2. This demonstrates that the coating composition of the present invention inhibits the availability of the drug ingredient and thereby provides an effective means for masking the undesirable taste of a drug ingredient such as APAP or caffeine under neutral pH conditions, but provides rapid release of the drug ingredient in an acidic environment.

10

#### EXAMPLE 2

Coating (B) made of 27.78% KOLLIDONE SR, 27.78% Ethyl Cellulose, 28.0% Eudragit E® 100, 8.44% EASTMAN 9-45 (Acetylated Monoglyceride), 3.0% Triethanolamine, and 5% Talc was applied to a drug ingredient, such as granules of acetaminophen (APAP) or caffeine powder. The coated drug ingredient was then compressed into tablet form, forming medicinal tablets that were then subjected to dissolution testing in solutions having a pH of 7 and a pH of 1.2.

15  
20

Tables 3 and 4 show the percentage of a drug ingredient dissolved over a given period of time in an environment where the pH is about 7, i.e. conditions similar to the mouth, and in

an environment where the pH is about 1.2, i.e. conditions similar to the stomach.

**TABLE 3**

**APAP with 30% Coating Add On of Coating B**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	1.5	4.5
6	11.8	56.3
11	17.5	81
16	21.8	91.8
21	28.8	96.4
26	35.1	98.1
31	41.6	98.9
36	47.9	99.3

**TABLE 4**

**Caffeine with 30% Coating Add On of Coating B**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	0.9	6.6
6	12	84.9
11	19	93.4
16	19.7	94.2
21	35.1	95
26	43.6	95.2
31	52.1	95.4
36	59.2	95.5

The results indicate that dissolution is hindered by coating (B), in an environment where the pH is about 7, and dissolution is quicker in an environment where the pH is about

1.2. This demonstrates that the coating composition of the present invention inhibits the availability of the drug ingredient and thereby provides an effective means for masking the undesirable taste of a drug ingredient such as APAP or  
5 caffeine under neutral pH conditions, but provides rapid release of the drug ingredient in an acidic environment.

### EXAMPLE 3

10 Coating (C) made of 60.0% SENTRY BG-75 Pure PVA, 32.0% EUDRAGIT® E 100, 3.0% Triethanolamine, and 5% Talc was applied to a drug ingredient, such as granules of acetaminophen (APAP) or caffeine powder. The coated drug ingredient was then compressed into tablet form, forming medicinal tablets that were  
15 then subjected to dissolution testing in solutions having a pH of 7 and a pH of 1.2.

Tables 5 and 6 show the percentage of a drug ingredient dissolved over a given period of time in an environment where  
20 the pH is about 7, i.e. conditions similar to the mouth, and in an environment where the pH is about 1.2, i.e. conditions similar to the stomach.

**TABLE 5****APAP with 30% Coating Add On of Coating C**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	0.8	1.3
6	11.1	14.7
11	17.3	22
16	22.4	27.5
21	26.9	32.2
26	31	36.2
31	35	39.9
36	38.5	43.4

5

**TABLE 6****Caffeine with 30% Coating Add On of Coating C**

TIME (min)	Dissolution at pH = 7	Dissolution at pH = 1.2
0	0	0
1	1.1	3.1
6	13.6	24.7
11	23.3	36
16	31	43.8
21	37.8	49.8
26	43.4	55
31	49	59.7
36	52.9	64.1

10        The results indicate that dissolution is hindered by coating (B), in an environment where the pH is about 7, and dissolution is quicker in an environment where the pH is about 1.2. This demonstrates that the coating composition of the present invention inhibits the availability of the drug

ingredient and thereby provides an effective means for masking the undesirable taste of a drug ingredient such as APAP or caffeine under neutral pH conditions, but provides rapid release of the drug ingredient in an acidic environment.

5

Having thus described the present invention with particular reference to preferred embodiments thereof, it will be apparent that various changes and modifications may be made therein without departing from the spirit and scope of the present  
10 invention as defined in the appended claims.

**WHAT IS CLAIMED IS:**

1. A coating composition for masking the taste of an ingredient comprising:
  - 5 (a) polyvinyl acetate; and
  - (b) dimethylaminoethyl methacrylate and neutral methacrylic acid ester.
- 10 2. The composition of claim 1, wherein said polyvinyl acetate is about 3 wt.% to about 97 wt.% of the total weight of the composition.
- 15 3. The composition of claim 1, wherein said dimethylaminoethyl methacrylate and neutral methacrylic acid ester is about 3 wt.% to about 97 wt.% of the total weight of the composition.
- 20 4. The composition of claim 1, further comprising an additive selected from the group consisting of 2-vinyl pyridine (V)/styrene (S) copolymer, ethyl cellulose, and mixtures thereof.
5. The composition of claim 1, further comprising one or more optional ingredients selected from the group consisting of



diluents, fillers, bulking agents, pigments, opacifiers, other plasticizers, processing aids, and mixtures thereof.

6. The composition of claim 5, wherein said processing  
5 aid is selected from the group consisting of sodium lauryl sulfate, colloidal silica, silicon dioxide, and mixtures thereof.

7. The composition of claim 1, further comprising an  
10 alkaline modifier.

8. The composition of claim 7, wherein said alkaline  
modifier is selected from the group consisting of  
triethanolamine, basic amino acids, talc, ammonium oleate,  
15 meglumine, trimethylamine, calcium silicate, aluminum magnesium silicate, food alkalizing agents, and mixtures thereof.

9. A coating composition for masking the taste of a drug  
ingredient or medicine and for enhancing controlled release of  
20 the drug or medicine, comprising:

- (a) polyvinyl acetate;
- (b) dimethylaminoethyl methacrylate and neutral methacrylic acid ester; and
- (c) an alkaline modifier.

10. The composition of claim 9, wherein said polyvinyl acetate is about 3 wt.% to about 97 wt.% of the total weight of the composition.

5

11. The composition of claim 9, wherein said dimethylaminoethyl methacrylate and neutral methacrylic acid ester is about 3 wt.% to about 97 wt.% of the total weight of the composition.

10

12. The composition of claim 9, wherein said alkaline modifier is selected from the group consisting of triethanolamine, basic amino acids, talc, ammonium oleate, meglumine, trimethylamine, calcium silicate, aluminum magnesium  
15 silicate, food alkalizing agents, and mixtures thereof.

13. The composition of claim 12, wherein said alkaline modifier is triethanolamine.

20

14. The composition of claim 9, wherein said alkaline modifier is about 0.2 wt.% to about 20 wt.% of the total weight of the composition.

15. The composition of claim 14, wherein said alkaline modifier is about 1 wt.% to about 15 wt.% of the total weight of the composition.

5        16. The composition of claim 9, further comprising an additive selected from the group consisting of 2-vinyl pyridine (V)/styrene (S) copolymer, ethyl cellulose, and mixtures thereof.

10       17. The composition of claim 9, further comprising one or more optional ingredients selected from the group consisting of diluents, fillers, bulking agents, pigments, opacifiers, other plasticizers, processing aids, and mixtures thereof.

15       18. The composition of claim 9, wherein said composition effectively masks the taste of the drug ingredient.

19. A medicament comprising:

an effective amount of a drug ingredient; and

20       a coating composition for masking the taste of the drug ingredient comprising:

(a) polyvinyl acetate; and

(b) dimethylaminoethyl methacrylate and neutral methacrylic acid ester, wherein said coating composition coats the drug ingredient.

5        20. The medicament of claim 19, wherein the drug ingredient is selected from the group consisting of particles, granules, powders, and mixtures thereof.

10       21. The medicament of claim 19, wherein said polyvinyl acetate polymer is about 3 wt.% to about 97 wt.% of the total weight of the composition.

15       22. The medicament of claim 19, wherein said dimethylaminoethyl methacrylate and neutral methacrylic acid ester is about 3 wt.% to about 97 wt.% of the total weight of the composition.

20       23. The medicament of claim 19, further comprising an additive selected from the group consisting of ethyl cellulose, polyvinylpyrrolidone, 2-vinyl pyridine (V)/styrene (S) copolymer, and mixtures thereof.

24. The medicament of claim 19, further comprising one or more optional ingredients selected from the group consisting of

diluents, fillers, bulking agents, pigments, opacifiers, other plasticizers, processing aids, and mixtures thereof.

25. The medicament of claim 19, further comprising an  
5 alkaline modifier to enhance controlled release of the drug or medicine.

26. The medicament of claim 25, wherein said alkaline  
modifier is selected from the group consisting of  
10 triethanolamine, basic amino acids, talc, ammonium oleate,  
meglumine, trimethylamine, calcium silicate, aluminum magnesium  
silicate, food alkalizing agents, and mixtures thereof.

27. The medicament of claim 25, wherein said alkaline  
15 modifier is about 0.2 wt.% to about 20 wt.% of the total weight  
of the composition.

28. The medicament of claim 25, wherein said alkaline  
modifier is about 2 wt.% to about 4 wt.% triethanolamine, and  
20 about 4 wt.% to about 8 wt.% other alkaline modifiers.

29. The medicament of claim 19, wherein the drug  
ingredient is selected from the group consisting of  
acetaminophen, aspirin, ibuprofen, dexibuprofen lysinate,

naproxen, ketoprofen, lactam, quinolone, macrolide and salts thereof, loperamide, famotidine, ranitidine, cimetidine and salts thereof, ibersartan, captopril, lisinopril and salts thereof, nefzodone, buspirone and salts thereof,  
5 chlorpheniramine, astemizole, pseudoephedrine, statins, antivirals, anticancer, antiplatelet, vitamins, minerals, psyllium, and mixtures thereof.

30. The medicament of claim 19, wherein said medicament is  
10 selected from the group consisting of: chewable tablets, powders for reconstituted suspensions, regular liquid form of prepared suspensions, fast dissolving quick melt tablets, lozenges, wafers, chewing gums, hard shell gelatin capsules with powder/granules/liquid fills, soft shell gelatin with liquid  
15 center or filled with powder or granules, regular compressed tablets with immediate or delayed release, candy and candy bar forms, aerosol creams, and gels.

31. The medicament of claim 19, wherein the medicament is  
20 a tablet formed by compressing coated granules.

32. The medicament of claim 19, wherein the medicament has a ratio of coating composition to drug ingredient that is about 1:50 to 3:1.

33. The medicament of claim 31, wherein said ratio is about 1:10 to 2:1.

5 34. A medicament comprising:

an effective amount of a drug ingredient; and  
a coating composition for masking the taste of the drug ingredient and enhancing the controlled release of the drug ingredient, comprising:

10 (a) polyvinyl acetate in an amount about 3 wt.% to about 97 wt.% of the total weight of the composition;

(b) dimethylaminoethyl methacrylate and neutral methacrylic acid ester in an amount about 3 wt.% to about 97 wt.% of the total weight of the composition; and

15 (c) an alkaline modifier in an amount about 0.2 wt.% to about 20 wt.% of the total weight of the composition.

(d) an additive selected from the group consisting of polyvinylpyrrolidone, 2-vinyl pyridine (V)/styrene (S) copolymer, ethyl cellulose, and mixtures thereof, wherein  
20 said coating composition coats the drug ingredient.

35. The medicament of claim 34, wherein the medicament has a ratio of coating composition to drug ingredient that is about 1:50 to 3:1.

36. The medicament of claim 35, wherein said ratio is about 1:10 to 2:1.

5 37. A medicament comprising:

an effective amount of a drug ingredient; and  
a coating composition for masking the taste of the drug ingredient and enhancing the controlled release of the drug ingredient, comprising:

10 (a) polyvinyl acetate in an amount about 28 wt.% of the total weight of the composition;

(b) dimethylaminoethyl methacrylate and neutral methacrylic acid ester in an amount about 28 wt.% of the total weight of the composition; and

15 (c) ethyl cellulose in an amount about 28 wt.% of the total weight of the composition;

(d) talc in an amount about 5 wt.% of the total weight of the composition;

(e) other alkaline modifiers in an amount about  
20 3 wt.% to about 11 wt.% of the total weight of the composition, wherein said coating composition coats the drug ingredient.



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
1 November 2001 (01.11.2001)

PCT

(10) International Publication Number  
**WO 01/80829 A3**

- (51) International Patent Classification<sup>7</sup>: A61K 9/56, 9/50
- (21) International Application Number: PCT/US01/12805
- (22) International Filing Date: 19 April 2001 (19.04.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
09/553,513 20 April 2000 (20.04.2000) US
- (71) Applicant: **BRISTOL-MYERS SQUIBB COMPANY**  
[US/US]; P.O. Box 4000, Route 206 and Provinceline  
Road, Princeton, NJ 08543-4000 (US).
- (72) Inventors: **CORBO, Michael**; 17 Litton Road, Flemington, NJ 08822 (US). **DESAI, Jatin**; 2009 Pheasant Hollow Drive, Plainsboro, NJ 08536 (US). **PATELL, Mahesh**; 4 Farrington Street, Edison, NJ 08820 (US). **WARRICK, Ronald**; 42 Route 523 South, Sergeantsville, NJ 08557 (US).
- (74) Agent: **KRIEGER, Stuart**; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
21 March 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 01/80829 A3

(54) Title: TASTE MASKING COATING COMPOSITION

(57) Abstract: There is provided a coating composition that masks the undesirable taste of a pharmaceutically active ingredient, i.e. drug or medicine, that is consumed orally. The coating composition has polyvinyl acetate, and a dimethylaminoethyl methacrylate and neutral methacrylic acid ester. Optionally, an alkaline modifier may be included in the coating composition to enhance release of the active ingredient.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/12805

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K9/56 A61K9/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 118 999 A (BEECHAM GROUP LTD) 4 August 1972 (1972-08-04) page 1, line 10 - line 16 page 2, line 36 -page 3, line 8 page 3, line 31 -page 4, line 15 page 4, line 29 -page 5, line 11 page 8, line 17 - line 18 page 8, line 25; examples 1-26 ---	1-37
A	EP 0 378 137 A (KALI CHEMIE PHARMA GMBH) 18 July 1990 (1990-07-18) page 2, line 15 - line 31 page 3, line 18 - line 39 page 4, line 10 - line 18 page 4, line 52 -page 5, line 35; claims; examples 2-5 --- -/--	1-37

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

17 December 2001

Date of mailing of the international search report

27/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Marttin, E

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/12805

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>EP 1 110 544 A (BASF AG)  27 June 2001 (2001-06-27)  the whole document  -----</p>	1-37

# INTERNATIONAL SEARCH REPORT

Information on patent family members

I. International Application No

PCT/US 01/12805

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
FR 2118999	A	04-08-1972	AU 3701671 A	21-06-1973
			BE 777158 A1	22-06-1972
			DE 2164019 A1	03-08-1972
			FR 2118999 A5	04-08-1972
			NL 7117616 A	27-06-1972
			ZA 7108014 A	30-08-1972
EP 0378137	A	18-07-1990	DE 3900811 A1	19-07-1990
			EP 0378137 A2	18-07-1990
			HU 52369 A2	28-07-1990
			JP 2288821 A	28-11-1990
EP 1110544	A	27-06-2001	DE 19961897 A1	28-06-2001
			CN 1300590 A	27-06-2001
			EP 1110544 A2	27-06-2001
			JP 2001172201 A	26-06-2001
			US 2001007680 A1	12-07-2001